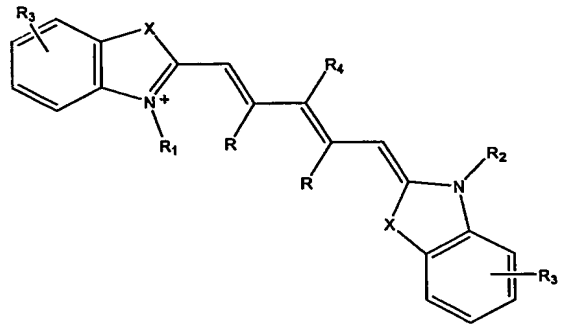
Claims

1. A reagent comprising a targeting moiety that selectively localizes to cells or tissue undergoing cell death, the targeting moiety being covalently conjugated to an infrared fluorescent substance.

2. The reagent according to claim 1, wherein the infrared fluorescent substance is a near-infrared fluorescent dye having a structure of the formula:



wherein, as valence and stability permit,

X represents $C(R)_2$, S, Se, O, or NR_5;

R represents H or lower alkyl, or two occurrences of R, taken together, form a ring together with the carbon atoms through which they are connected;

R_1 and R_2 represent, independently, substituted or unsubstituted lower alkyl, lower alkenyl, cycloalkyl, cycloalkylalkyl, aryl, or aralkyl, optionally substituted by sulfate, phosphate, sulfonate, phosphonate, halogen, hydroxyl, amino, cyano, nitro, carboxylic acid, or amide, or a pharmaceutically acceptable salt thereof;

R_3 represents, independently for each occurrence, one or more substituents to the ring to which it is attached, such as a fused ring, sulfate, phosphate, sulfonate, phosphonate, halogen, lower alkyl, hydroxyl, amino, cyano, nitro, carboxylic acid, or amide, or a pharmaceutically acceptable salt thereof;

R_4 represents H, halogen, or a substituted or unsubstituted ether or thioether of phenol or thiophenol; and

R_5 represents, independently for each occurrence, substituted or unsubstituted lower alkyl, cycloalkyl, cycloalkylalkyl, aryl, or aralkyl, optionally substituted by

sulfate, phosphate, sulfonate, phosphonate, halogen, hydroxyl, amino, cyano, nitro, carboxylic acid, amide, etc., or a pharmaceutically acceptable salt thereof.

3. A method of imaging cell death comprising
(a) contacting a sample of cells with a reagent of claim 1 or 2,
(b) positioning the sample adjacent to an electronic imaging device, and
(c) constructing an image of emission wavelength,
wherein said image is a representation of cell death in said sample.

4. A pharmaceutical preparation comprising a reagent of claim 1 or 2 and a pharmaceutically acceptable excipient.

5. A composition comprising a reagent of claim 1 or 2.

6. The reagent according to claim 1 or 2, wherein the targeting moiety is a protein or a fragment thereof.

7. The reagent according to claim 1, 2 or 6, wherein the targeting moiety is a protein, or a fragment thereof, having an amino acid sequence at least 60% homologous to the amino acid sequence of an annexin protein.

8. The reagent according to claim 7, wherein the protein, or fragment thereof, has at least one biological activity of an annexin protein, such as having a high affinity for anionic phospholipids surfaces.

9. The reagent according to claim 1, 2, or 6, wherein the targeting moiety is annexin V.

10. The reagent according to claim 1 or 6, wherein the fluorescent substance is a quantum dot.

11. The reagent according to claim 10, wherein the infrared fluorescent substance is a quantum dot and the targeting moiety is annexin V.

12. The reagent according to claim 1, 2, or 6, wherein the infrared fluorescent substance is iodocyanine green, IRDye78, IRDye80, IRDye38, IRDye40, IRDye41, IRDye700, IRDye800, Cy7, IR-786, DRAQ5NO, or analogs thereof.

13. The reagent according to claim 12, wherein the targeting moiety is annexin V and the infrared fluorescent substance is IRDye78 or an analog thereof.

14. The reagent according to claim 1, 2, or 6, wherein the infrared fluorescent substance/targeting moiety conjugate is purified from unconjugated infrared fluorescent substance through gel filtration or dialysis.

15. The reagent according to claim 1, 2, or 6, wherein the infrared fluorescent substance/targeting moiety conjugate is soluble in blood.

16. The reagent according to claim 1, 2, or 6, wherein the infrared fluorescent substance/targeting moiety conjugate is used to image organ and bone marrow transplant rejection or injury, infectious and non-infectious inflammatory diseases, autoimmune disease, cerebral and myocardial infarction and ischemia, cardiomyopathies, atherosclerotic disease, neural and neuromuscular degenerative diseases, sickle cell disease, β-thalassemia, cancer therapy, AIDS, myelodysplastic syndromes, such as aplastic anemia, toxin-induced liver disease, traumatic injury, bacterial infection, or acute hypoxia.

17. The reagent according to claim 1, 2, or 6, wherein the infrared fluorescent substance/targeting moiety conjugate is used to image ischemic injury.

18. The reagent according to claim 17, wherein the ischemic injury is myocardial infarction, reperfusion injury or stroke.

19. A method of imaging cell death within a region in vivo, comprising
(a) administering to a subject a preparation of claim 4,
(b) positioning the region adjacent to an electronic imaging device, and
(c) constructing an image of emission wavelength,
wherein said image is a representation of cell death within a region of said subject.

20. The method according to claim 19, wherein the electronic imaging device captures an image of a field of view that includes some portion of the subject, the image including a first image obtained from the one or more wavelengths of visible light and a second image obtained from the emission wavelength.

21. The method according to claim 19, wherein the electronic imaging device captures a visible light image of the surgical field and an emission wavelength image of the surgical field.

22. The method according to claim 19, wherein the electronic imaging device captures an image of a field of view that includes some portion of the subject, the image including a first image obtained from the one or more wavelengths of visible light and a second image concurrently obtained from the emission wavelength.

23. The method according to claim 19, wherein the preparation is administered intravenously, intraperitoneally, intrathecally, intrapleurally, intralymphatically, intravaginally, intravesically, intrarectally, or intramuscularly.

24. The method according to claim 19, wherein the preparation is topically applied to the region.

25. The method according to claim 19, wherein the preparation is administered in a dose of less than 300 μg protein/kg.

26. The method according to claim 19, wherein the preparation is administered in a dose of less than 50 μg protein/kg.

27. The method according to claim 19, wherein the preparation is administered in a dose of less than 10 μg protein/kg.

28. A method for detecting cell death in a cell sample or tissue sample, comprising

(a) treating the sample with a reagent of claim 1, 2, or 6,

(b) irradiating the sample with a light source,

(c) detecting an emission wavelength of the infrared fluorescent substance.

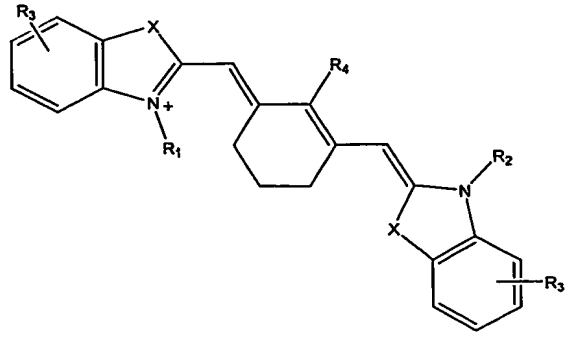
29. The reagent according to claim 1 or 2, wherein the fluorescent substance will have an emission wavelength in a range from about 680 nm to about 100,000 nm.

30. The reagent according to claim 1 or 2, wherein the fluorescent substance will have an emission wavelength in a range from about 680 nm to about 20,000 nm,

31. The reagent according to claim 1 or 2, wherein the fluorescent substance will have an emission wavelength in a range from about 700 nm to about 1,000 nm.

32. The reagent according to claim 2, wherein two occurrences of R taken together form a six-membered ring.

33. The reagent according to claim 1, wherein the infrared fluorescent substance is a near-infrared fluorescent dye having a structure of the formula:



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34. The reagent according to claim 32, wherein the near-infrared fluorescent dye is selected from IRDye78, IRDye80, IRDye38, IRDye40, IRDye41, IRDye700, IRDye800, Cy7, and compounds formed by conjugating a second molecule to any of IRDye78, IRDye80, IRDye38, IRDye40, IRDye41, IRDye700, IRDye800, and Cy7.